REMARKS

Previously, claims 1-5 were withdrawn from consideration and elected claims 6-14 were pending. In the instant amendment, non-elected claims 1-5 have been canceled without prejudice as discussed below. Claims 6-8 have been amended. After entry of the instant amendment, claims 6-14 will be pending and under consideration.

I. AMENDMENT TO THE SPECIFICATION

The first paragraph following the title has been amended to recite priority under 35 U.S.C. § 119(a)-(c) to European Application No. 01 105 172.9, filed March 2, 2001. This amendment is supported by the application and transmittal papers as filed (*see* "Patent Application Fee Value" sheet). Since this amendment is supported by the application and transmittal papers as filed, and the claim has been acknowledged by the Patent Office with a certified copy of the priority document received by the Patent Office (*see* page 2, paragraph 2, of the Office Action dated August 7, 2003), Applicants respectfully request entry of the amendment.

The specification has been amended at page 8 to correct punctuation marks and to capitalize the trademark "Wisconsin Package." As this amendment does not add new matter, entry thereof is respectfully requested.

II. AMENDMENT TO THE CLAIMS

Claims 1-5 have been canceled to conform to elected subject matter in Applicant's Response to Restriction Requirement, mailed April 17, 2003, without prejudice to Applicant's right to pursue non-elected subject matter in one or more related applications including divisional, continuation, or continuation-in-part applications.

Claims 6-8 have been amended to recite, in relevant part, "isolated control nucleic acid."

As the above amendments to claims are fully supported by the specification and claims as originally filed, entry thereof is respectfully requested. No new matter has been added. No amendment fee is believed to be due.

III. DISCLOSURE STATEMENT

The Patent Office has not considered four references, European Patent Nos. 0286028, 0324474, 0624161, and 0680969, that were cited in the information disclosure statement mailed October 1, 2002, since no translation of the four documents was provided.

Pursuant to 37 C.F.R. § 1.98(a)(3)(i) and (ii), an information disclosure statement shall include either a concise explanation of the relevance of a document not in the English language or else a copy of the translation if a written English-language translation of a non-English-language document, or portion thereof, is within the possession, custody, or control of, or is readily available to any individual designated in § 1.56(c). To fulfill the requirement for a concise explanation of the relevance for non-English language information, submission of an English language abstract of a reference may be used. MPEP § 609(III)(A)(3). There is no requirement that the translation be verified. *Id.*

English-language translations of the abstracts are readily available from the European Patent Office ("EPO") patent databases. Therefore, Applicants have enclosed four English-language translations of the abstracts of the cited European patents from the European Patent Office ("EPO") patent databases. Furthermore, in obtaining these abstracts, Applicants noted that certain U.S. patents correspond to European Patent Nos. 0286028, 0324474, and 0624161. For consideration of the information disclosed in the European Patent Nos. 0286028, 0324474, 0624161, and 0680969, Applicants enclose the following documents:

(1) a copy of the EPO's English-language translation of the abstract of European Patent No. 0286028 (*see* **EXHIBITS**; the chemical structure of formula I, indicated in the first line of the abstract, is shown on page 2, beginning at line 1, of EP 0286028, and the chemical structure of the group defining the second alternative for "W," indicated in the second line of the abstract, is shown in EP 0286028 at page 2, third line of text) and a copy of U.S. Patent No. 6,211,158, which corresponds to European Patent No. 0286028 (*see* Second Information Disclosure Statement);

(2) a copy of the EPO's English language translation of the abstract of European Patent No. 0324474 (*see* **EXHIBITS**) and copies of U.S. Patent Nos. 5,344,757 and 5,702,888, which correspond to European Patent No. 0324474 (*see* Second Information Disclosure Statement);

(3) a copy of the EPO's English language translation of the abstract of European Patent No. 0624161 (*see* **EXHIBITS**; the chemical structures of formulas I-VI, to which the abstract refers, are shown in Figure 1 of EP 0624161, and those of formulas a, b, and VII-IX are shown in Figure 2 of EP 0624161) and a copy of U.S. Patent Nos. 6,147,199, which corresponds to European Patent No. 0624161 (*see* Second Information Disclosure Statement); and

(4) a copy of the EPO's English language translation of the abstract of European Patent No. 0680969 (*see* **EXHIBITS**; the chemical structure of formula I, named in the first line of the abstract, is shown on page 2, lines 40-55, of EP 0680969).

IV. OBJECTIONS TO THE SPECIFICATION

A. Priority Information

The Patent Office objects to the instant disclosure for not reciting priority information in the first sentence on the first page of the specification. Applicants submit that the instant amendment to the specification to recite priority information obviates the objection. Therefore, Applicants respectfully request that the objection to the specification be withdrawn.

B. Trademark Usage

The Patent Office objects to the instant disclosure for not capitalizing the trademark "Wisconsin Package" and not having appropriate accompanying generic terminology. Applicants submit that the instant amendment to the specification to capitalize the trademark and insert generic terminology following the trademark obviates the objection. Accordingly, Applicants respectfully request that the objection to the specification be withdrawn.

V. REJECTION OF CLAIMS 6-8 UNDER 35 U.S.C. § 101

Claims 6-8 stand rejected under 35 U.S.C. § 101 allegedly because the claimed invention is directed to a non-statutory subject matter. Specifically, the Patent Office contends that a control nucleic acid such as recited in claim 6 reads on a product of nature such as a mRNA. Applicants respectfully disagree with the position taken by the Patent Office.

The control nucleic acid recited in claim 6 comprises a sequence parallel complementary to a target nucleic acid region (or the complement thereof). The specification at page 8, lines 4-16, defines the term "parallel complementary" and provides the examples of SEQ ID NO: 1 and SEQ ID NO: 2 to help visualize what is meant by the term. For example, a control nucleic acid sequence is the parallel complement of a target nucleic acid region if the control nucleic acid sequence has a 5' to 3' sequence that is the reverse of the 5' to 3' sequence of the complement of the target nucleic acid region (or of the target nucleic acid region itself). Figure 1 of the specification illustrates that strands that are the reverse or parallel complement of each other cannot anneal or hybridize to each other. In contrast, for a

given nucleic acid sequence to anneal to its complementary nucleic acid sequence, the two nucleic acid strands must have an anti-parallel complementary orientation. *See, e.g.*, page 9 and Fig. 1.6 *in* Lewin, *Genes VII* (2000) (*see* **EXHIBITS**).

Therefore, recognizing that mRNA hybridizes to its template DNA from which the mRNA was transcribed indicates that mRNA is an anti-parallel complement, not parallel complement, to the template DNA. Hence, a control nucleic acid such as recited in claim 6 does not read on a product of nature such as a mRNA.

While it seems unlikely that the control nucleic acid of claim 6 actually reads on any product of nature, nonetheless, claims 6-8 have been amended as suggested by the Patent Office. Accordingly, Applicants respectfully request that the rejection of claims 6-8 under 35 U.S.C. § 101 be withdrawn.

VI. REJECTION OF CLAIMS 6-14 UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 6-14 stand rejected under 35 U.S.C. § 112, first paragraph, allegedly for lack of written description. Chiefly, the Patent Office alleges that the specification does not provide sufficient written description to support the genus encompassed by the claims nor are the species disclosed representative of the genus. Applicants respectfully disagree and submit that claims 6-14 are fully supported by the specification as filed. In particular, Applicants respectfully submit that the Patent Office misapprehends the term "parallel complementary" and therefore misses the mark on how one of skill would recognize a "control nucleic acid" as it is used in any one of claims 6-14.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Possession may be shown by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. *Regents of the University of California v. Eli Lilly*, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997); MPEP § 2163.02. Applicants respectfully submit that by describing a control nucleic acid sequence that is "parallel complementary" to a target nucleic acid region in the application as filed, Applicants have, in fact, conveyed to those skilled in the art that Applicants were in possession of the full scope of the invention.

The specification at page 8, lines 4-16, defines the term "parallel complementary" and provides the examples of SEQ ID NO: 1 and SEQ ID NO: 2 to help visualize what is meant by the term. For example, a control nucleic acid sequence is the parallel complement of a

target nucleic acid region if the control nucleic acid sequence has a 5' to 3' sequence that is the reverse of the 5' to 3' sequence of the complement of the target nucleic acid region (or of the target nucleic acid region itself). Figure 1 of the specification illustrates that strands that are the reverse or parallel complement of each other cannot anneal or hybridize to each other.

In contrast, for a given nucleic acid sequence to anneal to its complementary nucleic acid sequence, the two nucleic acid strands must have an anti-parallel complementary orientation. *See, e.g.*, page 9 and Fig. 1.6 *in* Lewin, *Genes VII* (2000) (*see* **EXHIBITS**).

The full scope of each of claims 6-14 is described by the specification as filed since specific sequences are not critical to the claimed invention so long as the control nucleic acid sequence is parallel complementary to the target nucleic acid. A control nucleic acid that is parallel complementary to a target nucleic acid region as recited in claims 4-16 is similar to a target nucleic acid region in many parameters such as GC-content, secondary structure, etc., but remains separately detectable, as discussed in the specification on page 6, line 23, to page 7, line 26.

With the teaching of the instant specification, those of ordinary skill in the art will recognize the structure of a parallel complementary control nucleic acid as recited in claims 6-14 given any target nucleic acid no matter what its sequence. Indeed, Applicants respectfully submit that those of skill in the art relying upon the disclosure of the instant specification, for instance, on page 4, lines 2-12, page 6, lines 23-26, page 8, lines 4-16, and Figure 1, will recognize not only that a parallel complementary control nucleic acid sequence has a specific structure based upon the particular 5′ to 3′ sequence of any given target nucleic acid whatever that target nucleic acid may be, but will further recognize that, unlike the anti-parallel complementary sequence that hybridizes to the target nucleic acid sequence, the parallel complementary control nucleic acid sequence will mimic the properties of the target nucleic acid but will not interact or hybridize with the target nucleic acid. Since a specific recognizable parallel complementary nucleic acid, as described in the specification, exists for any target sequence, Applicants respectfully submit that the specification provides written description that fully supports the genus encompassed by the claims.

For the reasons discussed above, Applicants submit that the specification describes with reasonable clarity to those skilled in the art the distinguishing identifying characteristics to show that Applicants at the time of filing were in possession of the parallel complementary control nucleic acid of any of claims 6-14. Accordingly, Applicants respectfully request the withdrawal of the rejection of claims 6-14 under 35 U.S.C. § 112, first paragraph.

VII. REJECTION OF CLAIMS 6-12 UNDER 35 U.S.C. § 102(b)

Claims 6-12 stand rejected under 35 U.S.C. § 102(b), allegedly as being anticipated by Mullis (US 4,683,202, issued July 28, 1987). Claims 6, 8, 9, and 11 stand rejected under 35 U.S.C. § 102(b), allegedly as being anticipated by Nadeau *et al.* (US 5,840,487, issued November 24, 1998). Claims 6, 7, 9, 10 and 12-14 stand rejected under 35 U.S.C. § 102(b), allegedly as being anticipated by Tsang *et al.* (US 5,837,442, issued November 17, 1998).

For a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference. *See In re Bond*, 15 U.S.P.Q.2d 1566, 1567 (Fed. Cir. 1990). Applicants respectfully submit that not one of the references cited by the Patent Office teaches or suggests a control nucleic acid that comprises at least one contiguous sequence of at least 8 nucleotides in length essentially parallel complementary to a target nucleic acid region such as recited in claim 6.

From the outset, Applicants respectfully submit the importance of the meaning of term "parallel complementary" in understanding why none of the references anticipates any one of claims 6-12. Briefly, as discussed above in Section VI, the specification explains that a first nucleic acid is the parallel complement to a second nucleic acid if the sequence of the first nucleic acid is identical with the reversed sequence of the complementary strand of the second nucleic acid. Parallel complementary sequences do not hybridize or anneal together (*e.g.*, as shown in Figure 1 of the specification), since two sequences must be anti-parallel (not parallel) complementary sequences to each other to allow hybridization or annealing (*e.g.*, as shown on page 9 and Fig. 1.6 *in* Lewin, *Genes VII* (2000) (*see* **EXHIBITS**)).

A. Rejection of Claims 6-12 Under 35 U.S.C. § 102(b), Allegedly As Being Anticipated by Mullis

Claims 6-12 stand rejected under 35 U.S.C. § 102(b), allegedly as being anticipated by Mullis (US 4,683,202, issued July 28, 1987). The Patent Office cites three passages from Mullis as allegedly teaching a control nucleic acid sequence comprising a sequence that, according to the Patent Office, is essentially parallel complementary to a target nucleic acid region. Applicants respectfully disagree since Mullis features the use of primers that hybridize to their target nucleic acid. The primers have an anti-parallel, not parallel, complementary orientation to one or another DNA strand of a target nucleic acid.

For example, Mullis at column 15, lines 45-56, features the amplification of a 25 base pair double-stranded DNA sequence, wherein the strands are in an anti-parallel complementary orientation relative to each other, that is contained in a larger 47 base pair

restriction fragment. The eleven base primer and thirteen base primer taught at lines 55-56 each hybridize to one or the other of the single-stranded 25 base pair DNA strands. No parallel complementary control nucleic acid as recited in claims 6-12 is taught or suggested by Mullis at column 15, lines 45-56.

Furthermore, Mullis at example 5, column 20, lines 16-23, presents two oligonucleotides that, other than the three mismatches, are anti-parallel complementary to each other. Note that first oligonucleotide shown on line 18 begins with "5′" and the second oligonucleotide on line 21 begins with "3′," indicating the anti-parallel orientation. No parallel complementary control nucleic acid as in claims 6-12 is taught or suggested by Mullis at example 5, column 20, lines 16-23.

Again, Mullis at column 21, lines 30-38, features a primer pair for amplification of a β-globin sequence from genomic DNA. To amplify the β-globin sequence, the primers featured in Mullis at column 21, lines 30-38, must anneal to local sequences within the larger β-globin sequence. Therefore, these primers featured in Mullis are anti-parallel (not parallel) complements to local sequences within the β-globin sequence. No parallel complementary control nucleic acid as recited in claims 6-12 is taught or suggested by Mullis at column 21, lines 30-38.

Because Mullis features anti-parallel complementary primers and oligonucleotides, Mullis does not teach or suggest each and every limitation in any one of claims 6-12. Accordingly, Applicants respectfully request that the rejection of claims 6-12 under 35 U.S.C. § 102(b) be withdrawn.

B. Rejection of Claims 6, 8, 9, and 11 Under 35 U.S.C. § 102(b), Allegedly As Being Anticipated by Nadeau *et al.*

Claims 6, 8, 9 and 11 stand rejected under 35 U.S.C. § 102(b), allegedly as being anticipated by Nadeau *et al.* (US 5,840,487, issued November 24, 1998). The Patent Office alleges that Nadeau *et al.* at column 8, lines 1-41, teaches a control nucleic acid comprising a sequence that, according to the Patent Office, is parallel complementary to the probe binding site of the target nucleic acid. Therefore, the Patent Office concludes, Nadeau *et al.* meets all the claimed limitations of claims 6, 8, 9 and 11 of the instant application. Applicants respectfully disagree.

Nadeau *et al.* at column 8, lines 1-41 teaches use of SEQ ID NO:1 as a control oligonucleotide sequence in amplification reactions for detection of *Mycobacterium tuberculosis* (Mtb) where the target sequence is SEQ ID NO:2. Neither SEQ ID NO:1 of

Nadeau *et al.*, nor any contiguous sequence of at least 8 nucleotides in length of SEQ ID NO:1, is parallel complementary to the target SEQ ID NO:2 of Nadeau *et al.* Indeed, the 13 to 14-base sequences at the 5′- and 3′-ends of SEQ ID NO:1 are identical (not complementary) to the sequences at the 5′- and 3′-ends, respectively, of SEQ ID NO:2. The remaining sequence of SEQ ID NO:1, between the end-most sequences, is neither identical nor complementary to that in SEQ ID NO:2, but a sequence similar in GC content to that in SEQ ID NO:2. Because the probe on line 41 of Nadeau *et al.*, SEQ ID NO:3, has a sequence that will bind to the control sequence SEQ ID NO:1, the sequence of the probe SEQ ID NO:3 is an anti-parallel complement to SEQ ID NO:1. This can be verified by comparing SEQ ID NO:3 to residues 29-43 of SEQ ID NO:1. No parallel complementary control nucleic acid as recited in claims 6-12 of the instant application is taught or suggested by Nadeau *et al.* Nadeau *et al.* does not teach or suggest a control nucleic acid comprising at least one contiguous sequence of at least 8 nucleotides in length essentially parallel complementary to a target nucleic acid region or to its complement.

Applicants submit that Nadeau *et al.* does not teach or suggest each and every limitation of claims 6, 8, 9 and 11. Hence, Applicants respectfully request that the rejection of claims 6, 8, 9 and 11 under 35 U.S.C. § 102(b) be withdrawn.

C. Rejection of Claims 6, 7, 9, 10 and 12-14 Under 35 U.S.C. § 102(b), Allegedly As Being Anticipated by Tsang *et al.*

Claims 6, 7, 9, 10 and 12-14 stand rejected under 35 U.S.C. § 102(b), allegedly as being anticipated by Tsang *et al.* (US 5,837,442, issued November 17, 1998). The Patent Office alleges that Tsang *et al.*, in column 5, lines 24-45, teaches a control nucleic acid sequence comprising at least one contiguous sequence of at least 8 nucleotides in length essentially parallel complementary, according to the Patent Office, to said target nucleic acid region. Applicants respectfully disagree.

Tsang *et al.* at column 5, lines 24-45, teaches an upstream primer for use in conjunction with one of two disclosed downstream primers for the amplification of HCV nucleic acid. As explained by Tsang *et al.*, these primers hybridize to relatively conserved regions with the 5′ untranslated region of the HCV genome and enable the amplification of nucleic acid from the known HCV isolates (col. 5, lines 28-33). Therefore, since these primers hybridize to the template HCV DNA, these primers must be anti-parallel (not parallel) complementary to the template HCV DNA. This is because two nucleic acid sequences must anti-parallel (not parallel) complementary in order to hybridize to each other.

See, e.g., page 9 and Fig. 1.6 *in* Lewin, *Genes VII* (2000) (*see* **EXHIBITS**). No parallel complementary control nucleic acid as recited in claims 6-12 of the instant application is taught or suggested by Tsang *et al.*

Applicants respectfully submit that Tsang *et al.* does not teach or suggest each and every limitation of claims 6, 7, 9, 10 and 12-14. Accordingly, Applicants respectfully request the withdrawal of the rejection of claims 6, 7, 9, 10 and 12-14 under 35 U.S.C. § 102(b).

CONCLUSION

In light of the above amendments and remarks, the Applicant respectfully requests that the Examiner reconsider this application with a view towards allowance. The Examiner is invited to call the undersigned attorney if a telephone call could help resolve any remaining items.

The Commissioner is hereby authorized to charge any required fee(s) to Pennie & Edmonds LLP U.S. Deposit Account No. 16-1150 (order no. 1803-335-999). A copy of this sheet is enclosed for such purpose.

Respectfully submitted,

Date: October 22, 2003

42,983

Rahul Pathak (Reg. No.)
For: Nikolaos C. George (Reg. No. 39,201)
PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

EXHIBITS 1-5

1. Copy of English language abstract of European Patent No. 0286028
2. Copy of English language translation of the abstract of European Patent No. 0324474
3. Copy of the English language translation of the abstract of European Patent No. 0624161
4. Copy of the English language translation of the abstract of European Patent No. 0680969.
5. Copies of the front and back of title page and pages 8 &9 of Lewin, *Genes VII* (Oxford University Press 2000).